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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/552,272	04/19/2000	Li Fang	913.6600CIP	3198

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EXAMINER	
EPPS FORD, JANET L	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/552,272	FANG ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 5-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 5-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2-06-04 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

3. Claims 1, 3, 5-14, and 16-57 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the Official Action mailed 11-19-02.

Applicant's arguments filed 11-25-03 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that the specification clearly demonstrates possession of the 5'-UTR of any of a number of cold shock inducible genes. According to Applicants, they have clearly described and enabled the 5'-UTR of *cspA, cspB, and csdA* genes, and demonstrate that they share a similar sequence, with this information Applicants argue that the skilled artisan can take this sequence information and "locate the 5'-UTR of any cold shock gene." They further argue that the written description requirement (reference is made

to a correlation of structure and function as described in *Enzo Biochem, Inc. vs. Gene-Probe, Inc., 63,* USPQ 2d 1609, 1623) is fulfilled because they have described the particular function of the claimed genetic material, have identified three exemplary genes and their UTR's, and correlated them to a particular function, namely mediation of cold shock expression. Applicants make reference to various portions of case law to support their assertion that the specification as filed need not disclose the sequence of each and every 5'-UTR, which mediates translation in order to satisfy the written description guidelines.

Applicant's arguments are not persuasive since the scope of the claims encompasses wherein the isolated nucleic acid molecule of the invention is a "portion" of a 5'-UTR of a cold shock inducible gene, and further wherein the nucleic acid molecule has substantial homology to particular nucleotides of SEQ ID NO: 55. However, Applicants have not defined the scope of the term "portion" therefore, the scope of the number of isolated nucleic acid molecules that are a "portion" of a 5'-UTR of a cold shock inducible gene is also undefined. Moreover, the instant claims are not drawn to nucleic acid molecules which comprise only a portion of the 5'-UTR disclosed in the specification as filed that are known to be associated with cold shock inducible genes, the scope of the instant claims encompasses isolated nucleic acid molecules that are "portions" of any particular 5'-UTR of any cold shock response gene found in any bacterium. Apart from the need for further experimentation, the information in the specification as filed regarding the structure of SEQ ID NO: 55, and the portions according to nucleotides 1-11, 56-117, and 125-135 of SEQ ID NO: 55, there is no other direct correlation between the full scope of nucleic acid sequences encompassed by the instant claims and the regulation of expression of a cold shock inducible gene under physiological conditions.

Additionally, the instant claims (in particular claims 5, 10, 14, and those claims dependent thereon) are drawn to nucleic acid molecules "having substantial homology to" nucleotides 1-11, 56-117, and nucleotides 123-135 of SEQ ID NO: 55. According to the specification as filed (see page 16, 3rd paragraph) the term "homologous" refers to molecules "which have substantially the same molecular sequence of the referenced nucleic acid sequence, but may contain additions, deletions, or substitutions. Homologous molecules are defined as those molecules which hybridize under low or high stringency conditions to a nucleic acid molecule that is precisely complementary to the referenced nucleic acid molecule and which performs the same function as the referenced nucleic acid." Therefore, the scope of the nucleic acid molecules having substantial homology to the recited nucleotides of SEQ ID NO: 55 encompass sequences containing an undefined number of additions, deletions, or substitutions. However, the specification as filed does not provide any guidance as to what additions, deletions, or substitutions can be made such that the claimed function is maintained.

Moreover, the instant claims read on "nucleic acid fragments" that function to enhance the translation of a cold shock inducible gene, it is noted that there is no reference to any particular sequence structure such that there is an obvious correlation between the claimed function and the corresponding nucleic acid sequence structure. It is noted that the instant claims read beyond regular control of translation to an enhancement of translation, therefore the skilled artisan is required to identify those sequences that produce above normal translational control.

It is clear that the further experimentation required identifying the full scope of the claimed invention due to the lack of a clear correlation between nucleotide sequence and regulation of the cold shock response. The additional experimentation would require the

identification of all cold shock inducible genes of bacterium, the identification of their 5'-UTR, site directed mutagenesis, and expression assays to determine what portion of the 5'-UTR remaining after mutagenesis is capable of regulating the cold shock response in a bacterium. There is no direct guidance that will allow the skilled artisan to predict the structures of the full scope of cold shock inducible genes of all bacterium, and furthermore to predict what nucleotide structures within the identified 5'-UTR is required to control the cold shock response.

See MPEP § 2163, which states "A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." Additionally, possession cannot be demonstrated by a means for isolating an invention, "[A]n applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was 'ready for patenting' such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that applicant was in possession of the claimed invention." See the January 5, 2001 (Vol. 66, No. 4, pages 1099-1111) Federal Register for the Guidelines for Examination of Patent Applications Under the 35 USC 112 ¶ 1.

As stated in the prior Office Action, the full scope of the claimed invention was not "ready for patenting" at the time the invention was filed. Therefore, applicant was not in

possession of the full scope of the claimed invention at the time of filing of the instant application.

Response to Arguments

4. Claims 1, 3, and 5-15 remain rejected, and claim 57 is rejected under 35 U.S.C. 102(b) as being anticipated by Goldstein et al. for the reasons of record set forth in the Official Action mailed 9-13-01.

Applicant's arguments filed 12-25-03 have been fully considered but they are not persuasive. Applicants traverse the instant claims on the grounds that Goldstein refers to the *cspA* gene and its promoter, which aids in the regulation of transcription, however Applicant's invention refers to a cold shock inducible gene whose expression is regulated by the 5'UTR of the cold shock gene. Contrary to Applicant's assertions, it is noted that the Goldstein et al. describes a probable Shine-Delgarno sequence located upstream of the coding region beginning at nucleotide 605. Additionally, Goldstein et al. provide preliminary evidence that the transcription start sites are located at positions 457, 458 and 508 by primer extension, however it appears that translation begins at nucleotide position 617 of the sequence described in Figure 5. Applicants appear to be inferring that possession of the DNA sequence does not suggest possession of the mRNA sequence. However, the sequence according to SEQ ID NO: 55 of the instant application, corresponding to the 5'UTR of *cspA* corresponds to nucleotides 462-623 of the sequence described in Figure 5 of Goldstein et al. the only difference is that Applicant's sequence is an mRNA sequence instead of the DNA sequence. It is clear that the Shine Delgarno sequence described by Goldstein et al. located at position 605 of Figure 5, falls within

nucleotides 462-623, and corresponds a portion of a 5'UTR of a cold shock inducible gene as claimed by Applicants.

5. Claims 1, 3, 5-6, and 57 remain rejected under 35 U.S.C. 102(b) as being anticipated by Oppenheim et al. (US Patent No. 5,726,039) or Oppenheim et al. (US Patent No. 5,654,169).

Applicant's arguments filed 12-25-03 have been fully considered but they are not persuasive. Applicants traverse the instant claims on the grounds that the "promoter fragment" used in the constructs of Oppenheim et al. do not comprise a 5'-UTR sequence. However, contrary to Applicant's assertions, it is noted that one of the promoter fragments disclosed by Oppenheim et al. comprise 449 nucleotides before the start codon, see Figure 19. A sequence of 449 nucleotides beyond the start codon undoubtedly comprises 5'-UTR sequence of the cspA gene, and furthermore this 5'-UTR sequence was able to drive the temporal cold-shock expression of lacZ. See, Figure 3 and Figure 9A of the specification as filed wherein Applicants used a transcription assay to determine various portions of the 5'-UTR sequence of *cspA* to identify those sequences responsible for controlling the cold shock response, this is the same type of experiment used by Oppenheim et al. to identify those nucleic acid sequences used to control the cold shock response of the 5'-UTR of the *cspA* gene. Applicant's arguments do not take the place of evidence; the instant claims remain rejected for the reasons of record.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 7-8, and 11-12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16-41 of U.S. Patent No. 5,981,280. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the issued US Patent are drawn to nucleic acid molecules that comprise a portion of a 5'-UTR of a cold shock inducible gene, a translational initiation codon and a down stream box, wherein said sequences inhibits protein translation in a bacterium under conditions of cold shock, and the claims of the pending application broadly encompass the nucleic acid molecules of the issued US Patent. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). The claims of the instant application are generic to all that is recited in the claims of the issued US Patent. For example, the instant claims are drawn to nucleic acid molecules that comprise a portion of a 5'UTR of a cold shock inducible gene, and fragments of nucleic acid sequences derived from a cold shock inducible gene. The claims of the issued US Patent fall entirely within the scope of

claims 7-8 and 11-12 or, in other words, claims 7-8, and 11-12 are anticipated by claim(s) 16-41 of U.S. Patent No. 5,981,280.

8. Claims 1, 3, 6-9, and 11-12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 45-49 of US Patent No. 6,686,174 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the issued US Patent are drawn to nucleic acid molecules that comprise at least part of the 5'UTR of a cold shock inducible gene, wherein the 5'UTR is of cspA, or csdA, and the claims of the pending application broadly encompass the isolated nucleic acid molecules that are a portion of a 5'UTR of a cold shock inducible gene. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). The claims of the instant application are generic to all that is recited in the claims of the issued US Patent. For example, the instant claims are drawn to nucleic acid molecules that comprise a portion of a 5'UTR of a cold shock inducible gene, and fragments of nucleic acid sequences derived from a cold shock inducible gene. The claims of the issued US Patent fall entirely within the scope of claim 1 or, in other words, claims 1, 3, 6-9, and 11-12 are anticipated by claim(s) 45-49 of U.S. Patent No. 6,686,174 B1.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Epps-Ford, Ph.D.
Examiner
Art Unit 1635

JLE